

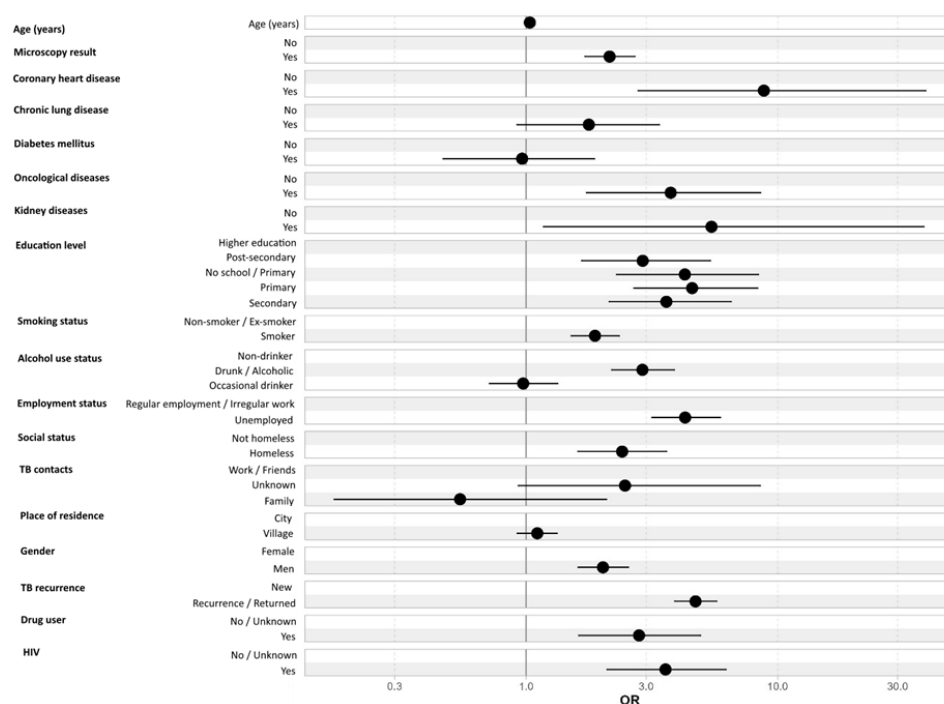


Figure S1 Univariate analysis of factors associated with drug-resistance pulmonary tuberculosis and unsuccessful treatment outcomes in Lithuania 2000–2007 (n=2,276). CI, confidence interval; HIV, human immunodeficiency virus; OR, odds ratio; TB, tuberculosis.

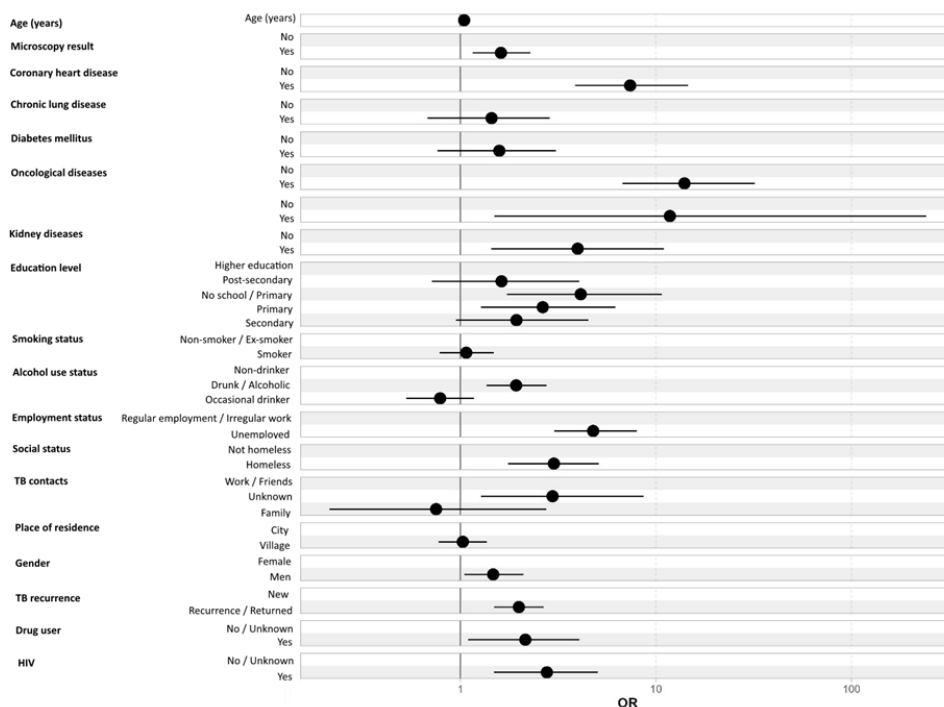


Figure S2 Univariate analysis of factors associated with drug-resistance pulmonary tuberculosis and unsuccessful treatment outcomes in Lithuania 2008–2015 (n=2,229). CI, confidence interval; HIV, human immunodeficiency virus; OR, odds ratio; TB, tuberculosis.

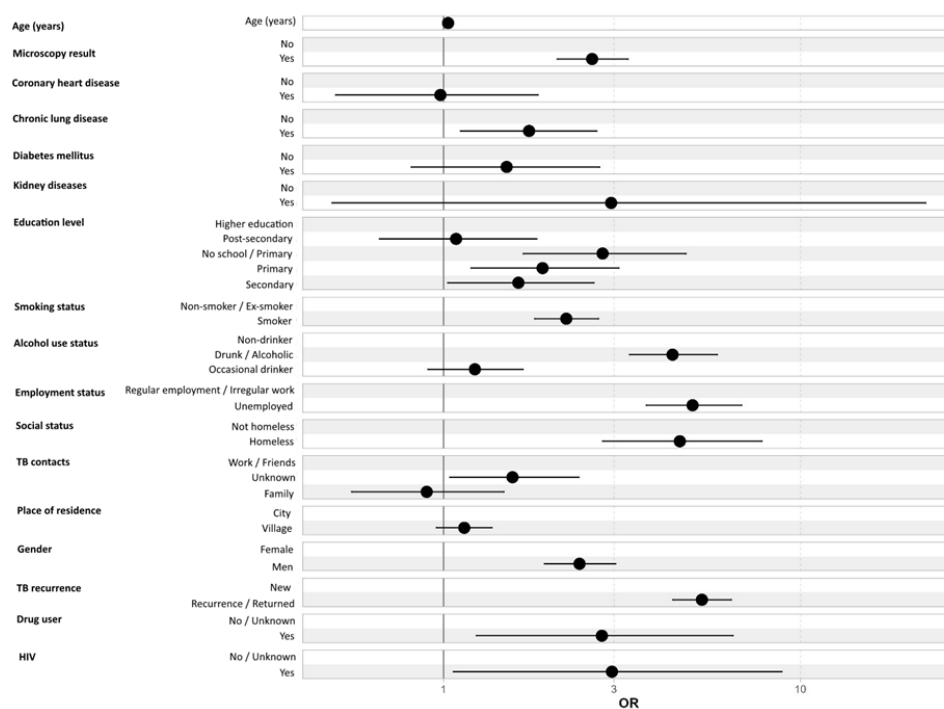


Figure S3 Univariate analysis of factors associated with drug-resistance pulmonary tuberculosis and unsuccessful treatment outcomes in Lithuania, 2016–2021 (n=1,256). CI, confidence interval; HIV, human immunodeficiency virus; OR, odds ratio; TB, tuberculosis.

Table S1 The WHO definitions are used for classifying TB cases

Term	Definition
Bacteriologically confirmed TB	TB case confirmed by positive smear microscopy, culture, or WHO-recommended rapid diagnostic tests (e.g., Xpert MTB/RIF)
Clinically diagnosed TB	TB case diagnosed based on clinical, radiological, or histological findings in the absence of bacteriological confirmation
New patient	A person who has never received TB treatment or has received it for less than one month
Relapse patient	A person previously treated for TB who was cured or completed treatment and is now diagnosed again, due to either relapse or reinfection

TB, tuberculosis; WHO, World Health Organization.

Table S2 Clinical characteristics of drug-resistance pulmonary tuberculosis cases in Lithuania, 2000–2021				
Variables	Period I (N=2,099)	Period II (N=1,869)	Period III (N=1,071)	P
Age (years), n (%)				0.187 ^a
[0, 40]	724 (34.5)	660 (35.3)	337 (31.5)	
(40, 50]	594 (28.3)	490 (26.2)	294 (27.5)	
(50, 60]	456 (21.7)	436 (23.3)	253 (23.6)	
(60, Inf]	325 (15.5)	283 (15.1)	187 (17.5)	
Age (years), n (%)				0.008 ^a
[0, 30]	304 (14.5)	300 (16.1)	124 (11.6)	
(30, 50]	1,014 (48.3)	850 (45.5)	507 (47.3)	
(50, max]	781 (37.2)	719 (38.5)	440 (41.1)	
Age (years), mean ± SD	46.4±14.4	46.2±14.9	47.6±14.4	0.031 ^b
Culture results, n (%)				>0.999 ^c
Negative	0	0	0	
Positive	2,099 (100.0)	1,869 (100.0)	1,071 (100.0)	
Microscopy results, n (%)				0.540 ^a
N	545 (26.0)	489 (26.2)	297 (27.7)	
P	1,554 (74.0)	1,380 (73.8)	774 (72.3)	
Coronary heart diseases, n (%)				<0.001 ^a
No	2,059 (98.1)	1,855 (99.3)	1,038 (96.9)	
Yes	40 (1.9)	14 (0.7)	33 (3.1)	
Chronic lung diseases, n (%)				<0.001 ^a
No	2,019 (96.2)	1,845 (98.7)	1,041 (97.2)	
Yes	80 (3.8)	24 (1.3)	30 (2.8)	
Diabetes mellitus, n (%)				0.005 ^a
No	2,060 (98.1)	1,833 (98.1)	1,033 (96.5)	
Yes	39 (1.9)	36 (1.9)	38 (3.5)	
Oncological diseases, n (%)				<0.001 ^a
No	2,096 (99.9)	1,849 (98.9)	1,037 (96.8)	
Yes	3 (0.1)	20 (1.1)	34 (3.2)	
Liver diseases, n (%)				0.010 ^c
No	2,099 (100.0)	1,865 (99.8)	1,067 (99.6)	
Yes	0	4 (0.2)	4 (0.4)	
Kidney diseases, n (%)				<0.001 ^a
No	2,094 (99.8)	1,862 (99.6)	1,058 (98.8)	
Yes	5 (0.2)	7 (0.4)	13 (1.2)	
Education, n (%)				<0.001 ^a
Higher education	103 (4.9)	120 (6.4)	68 (6.3)	
College/vocational	333 (15.9)	305 (16.3)	124 (11.6)	
Secondary	838 (39.9)	826 (44.2)	519 (48.5)	
Basic	619 (29.5)	504 (27.0)	307 (28.7)	
Primary/no formal	205 (9.8)	113 (6.0)	53 (4.9)	
Unknown	1	1	0	
Smoking, n (%)				0.184 ^a
Non-smoker/ex-smoker	653 (31.1)	540 (28.9)	305 (28.5)	
Smoker	1,445 (68.9)	1,329 (71.1)	766 (71.5)	
Unknown	1	0	0	
Alcohol consumption, n (%)				<0.001 ^a
Does not drink	381 (18.2)	310 (16.6)	299 (27.9)	
Drinks rarely	745 (35.5)	707 (37.8)	383 (35.8)	
Heavy drinker/alcoholic	972 (46.3)	852 (45.6)	389 (36.3)	
Unknown	1	0	0	
Employment status, n (%)				<0.001 ^a
Employed/irregular	427 (20.3)	377 (20.2)	283 (26.4)	
Unemployed	1,672 (79.7)	1,492 (79.8)	788 (73.6)	
Social status, n (%)				0.074 ^a
Not homeless	2,035 (97.0)	1,799 (96.3)	1,021 (95.4)	
Homeless	63 (3.0)	70 (3.7)	49 (4.6)	
Unknown	1	0	1	
TB contacts, n (%)				<0.001 ^a
Work/friends	121 (5.8)	21 (1.1)	57 (5.3)	
Family	247 (11.8)	128 (6.8)	88 (8.2)	
Unkown	1,731 (82.5)	1,720 (92.0)	926 (86.5)	
Place of residence, n (%)				0.005 ^a
Urban	1,329 (63.3)	1,133 (60.6)	615 (57.4)	
Rural	770 (36.7)	736 (39.4)	456 (42.6)	
Sex, n (%)				0.773 ^a
Female	520 (24.8)	481 (25.7)	273 (25.5)	
Male	1,579 (75.2)	1,388 (74.3)	798 (74.5)	
TB recurrence, n (%)				<0.001 ^a
New case	1,226 (58.4)	1,403 (75.1)	868 (81.0)	
Recurrence/relapse	873 (41.6)	466 (24.9)	203 (19.0)	
Substances user, n (%)				<0.001 ^a
No/unknown	2,076 (98.9)	1,824 (97.6)	1,032 (96.4)	
Yes	23 (1.1)	45 (2.4)	39 (3.6)	
HIV, n (%)				<0.001 ^a
No/unknown	2,088 (99.5)	1,817 (97.2)	1,031 (96.3)	
Yes	11 (0.5)	52 (2.8)	40 (3.7)	

^a, Pearson’s Chi-squared test; ^b, One-way analysis of means (ANOVA); ^c, Fisher’s exact test. Period I: 2000–2007; Period II: 2008–2015; Period III:2016–2021. HIV, human immunodeficiency virus; N, negative; P, positive; SD, standard deviation; TB, tuberculosis.

Table S3 Comparison of sociodemographic and clinical characteristics between patients with tuberculosis treatment failure and treatment success in Lithuania, 2000–2008

Variable	Treatment failure (N=769)	Treatment success (N=1,507)	P
Age (years), mean ± SD	49.9±12.6	44.1±14.7	<0.001 ^a
Culture result, n (%)			
P	769 (100.0)	1,507 (100.0)	
Microscopy results, n (%)			<0.001 ^b
N	113 (14.7)	467 (31.0)	
P	656 (85.3)	1,040 (69.0)	
Coronary heart disease, n (%)			0.950 ^b
No	755 (98.2)	1,479 (98.1)	
Yes	14 (1.8)	28 (1.9)	
Chronic pulmonary disease, n (%)			0.013 ^b
No	730 (94.9)	1,462 (97.0)	
Yes	39 (5.1)	45 (3.0)	
Diabetes mellitus, n (%)			0.183 ^b
No	750 (97.5)	1,482 (98.3)	
Yes	19 (2.5)	25 (1.7)	
Oncology, n (%)			0.038 ^c
No	766 (99.6)	1,507 (100.0)	
Yes	3 (0.4)	0	
Liver disease, n (%)			>0.999 ^c
No	769 (100.0)	1,507 (100.0)	
Yes	0	0	
Kidney disease, n (%)			0.343 ^c
No	766 (99.6)	1,505 (99.9)	
Yes	3 (0.4)	2 (0.1)	
Education, n (%)			<0.001 ^b
Higher education	25 (3.3)	81 (5.4)	
Colleague	93 (12.1)	278 (18.5)	
No schooling/primary	99 (12.9)	115 (7.6)	
Basic	249 (32.4)	426 (28.3)	
Secondary	303 (39.4)	606 (40.2)	
Unknown	0	1	
Smoking, n (%)			<0.001 ^b
Non-smoker/ex-smoker	154 (20.0)	536 (35.6)	
Smoker	615 (80.0)	970 (64.4)	
Unknown	0	1	
Alcohol, n (%)			<0.001 ^b
Alcoholic/abuser	523 (68.0)	539 (35.8)	
Non-drinker	72 (9.4)	325 (21.6)	
Rare use	174 (22.6)	642 (42.6)	
Unknown	0	1	
Employment status, n (%)			<0.001 ^b
Employed (regular)/irregular	51 (6.6)	394 (26.1)	
Unemployed	718 (93.4)	1113 (73.9)	
Social status, n (%)			<0.001 ^b
Homeless	49 (6.4)	22 (1.5)	
Not homeless	720 (93.6)	1,484 (98.5)	
Unknown	0	1	
TB contacts, n (%)			<0.001 ^b
Work/friends	32 (4.2)	90 (6.0)	
Unknown	671 (87.3)	1,210 (80.3)	
Family	66 (8.6)	207 (13.7)	
HIV, n (%)			0.048 ^b
Negative/unkwon	760 (98.8)	1,501 (99.6)	
Yes	9 (1.2)	6 (0.4)	
Substance use, n (%)			0.001 ^b
No/unkwon	755 (98.2)	1,497 (99.3)	
Yes	14 (1.8)	10 (0.7)	
Place of residence, n (%)			0.145 ^b
Rural	299 (38.9)	539 (35.8)	
Urban	470 (61.1)	968 (64.2)	
Gender, n (%)			<0.001 ^b
Female	112 (14.6)	438 (29.1)	
Male	657 (85.4)	1,069 (70.9)	
TB case category, n (%)			<0.001 ^b
New	247 (32.1)	1,077 (71.5)	
Relapse/return	522 (67.9)	430 (28.5)	
Tuberculosis resistance, n (%)			<0.001 ^b
Drug-resistance TB	155 (20.2)	932 (61.8)	
Multidrug-resistant TB	603 (78.4)	569 (37.8)	
Extensively drug-resistant TB	11 (1.4)	6 (0.4)	

^a, two sample *t*-test; ^b, Pearson's Chi-squared test. HIV, human immunodeficiency virus; N, negative; P, positive; SD, standard deviation; TB, tuberculosis.

Table S4 Comparison of sociodemographic and clinical characteristics between patients with tuberculosis treatment failure and treatment success in Lithuania, 2009–2015

Variables	Treatment failure (N=703)	Treatment success (N=1,526)	P
Age (years), mean ± SD	51.2±13.3	44.3±14.5	<0.001 ^a
Culture results, n (%)			
P	703 (100.0)	1,526 (100.0)	
Microscopy result, n (%)			<0.001 ^b
N	114 (16.2)	448 (29.4)	
P	589 (83.8)	1,078 (70.6)	
Coronary heart disease, n (%)			<0.001 ^c
No	691 (98.3)	1,523 (99.8)	
Yes	12 (1.7)	3 (0.2)	
Chronic pulmonary diseaselast, n (%)			0.077 ^b
No	686 (97.6)	1,505 (98.6)	
Yes	17 (2.4)	21 (1.4)	
Diabetes mellitus, n (%)			0.917 ^b
No	691 (98.3)	1,499 (98.2)	
Yes	12 (1.7)	27 (1.8)	
Oncology, n (%)			<0.001 ^b
No	686 (97.6)	1,516 (99.3)	
Yes	17 (2.4)	10 (0.7)	
Liver disease, n (%)			0.003 ^c
No	698 (99.3)	1,526 (100.0)	
Yes	5 (0.7)	0	
Kidney disease, n (%)			0.036 ^c
No	698 (99.3)	1,524 (99.9)	
Yes	5 (0.7)	2 (0.1)	
Education, n (%)			<0.001 ^b
Higher education	15 (2.1)	116 (7.6)	
College	100 (14.2)	266 (17.4)	
No schooling/primary	47 (6.7)	85 (5.6)	
Basic	224 (31.9)	379 (24.9)	
Secondary	317 (45.1)	679 (44.5)	
Unknown	0	1	
Smoking, n (%)			<0.001 ^b
Non-smoker/ex-smoker	131 (18.6)	459 (30.1)	
Smoker	572 (81.4)	1,067 (69.9)	
Alcohol, n (%)			<0.001 ^b
Alcoholic/abuser	470 (66.9)	619 (40.6)	
Non-drinker	72 (10.2)	275 (18.0)	
Rare use	161 (22.9)	632 (41.4)	
Employment status, n (%)			<0.001 ^b
Employed (regular)/irregular	49 (7.0)	371 (24.3)	
Unemployed	654 (93.0)	1,155 (75.7)	
Social satus, n (%)			<0.001 ^b
Homeless	51 (7.3)	48 (3.1)	
Not homeless	652 (92.7)	1,478 (96.9)	
TB contacts, n (%)			<0.001 ^b
Work/friends	4 (0.6)	20 (1.3)	
Unknown	686 (97.6)	1,387 (90.9)	
Family	13 (1.8)	119 (7.8)	
HIV, n (%)			<0.001 ^b
No/unknown	668 (95.0)	1,504 (98.6)	
Yes	35 (5.0)	22 (1.4)	
Substance use, n (%)			<0.001 ^b
No/unknown	674 (95.9)	1,503 (98.5)	
Yes	29 (4.1)	23 (1.5)	
Place of residence, n (%)			0.272 ^b
Rural	289 (41.1)	590 (38.7)	
Urban	414 (58.9)	936 (61.3)	
Gender, n (%)			<0.001 ^b
Female	114 (16.2)	429 (28.1)	
Male	589 (83.8)	1,097 (71.9)	
TB case category, n (%)			<0.001 ^b
New	290 (41.3)	1,172 (76.8)	
Relapse/return	413 (58.7)	354 (23.2)	
Tuberculosis resistance, n (%)			<0.001 ^b
Drug-resistance TB	145 (20.6)	846 (55.4)	
Multidrug-resistant TB	380 (54.1)	573 (37.5)	
Extensively drug-resistant TB	178 (25.3)	107 (7.0)	

^a, two sample *t*-test; ^b, Pearson's Chi-squared test. HIV, human immunodeficiency virus; N, negative; P, positive; SD, standard deviation; TB, tuberculosis.

Table S5 Comparison of sociodemographic and clinical characteristics between patients with tuberculosis treatment failure and treatment success in Lithuania, 2016–2021

Variable	Treatment failure (N=257)	Treatment success (N=999)	P
Age (years), mean ± SD	54.9±14.8	46.1±13.5	<0.001 ^a
Culture result, n (%)			
P	257 (100.0)	999 (100.0)	
Microscopy result, n (%)			0.004 ^b
N	53 (20.6)	295 (29.5)	
P	204 (79.4)	704 (70.5)	
Coronary heart disease, n (%)			<0.001 ^b
No	231 (89.9)	984 (98.5)	
Yes	26 (10.1)	15 (1.5)	
Chronic pulmonary disease, n (%)			0.304 ^b
No	246 (95.7)	969 (97.0)	
Yes	11 (4.3)	30 (3.0)	
Diabetes mellitus, n (%)			0.185 ^b
No	245 (95.3)	969 (97.0)	
Yes	12 (4.7)	30 (3.0)	
Oncology, n (%)			<0.001 ^b
No	228 (88.7)	990 (99.1)	
Yes	29 (11.3)	9 (0.9)	
Liver disease, n (%)			0.029 ^c
No	254 (98.8)	998 (99.9)	
Yes	3 (1.2)	1 (0.1)	
Kidney disease, n (%)			0.008 ^c
No	249 (96.9)	991 (99.2)	
Yes	8 (3.1)	8 (0.8)	
Education, n (%)			0.003 ^b
Higher education	8 (3.1)	66 (6.6)	
Colleague	25 (9.7)	127 (12.7)	
No schooling/primary	22 (8.6)	44 (4.4)	
Basic	87 (33.9)	272 (27.2)	
Secondary	115 (44.7)	490 (49.0)	
Smoking, n (%)			0.661 ^b
Non-smoker/ex-smoker	68 (26.5)	278 (27.8)	
Smoker	189 (73.5)	721 (72.2)	
Alcohol, n (%)			<0.001 ^b
Alcoholic/abuser	136 (52.9)	338 (33.8)	
Non-drinker	58 (22.6)	278 (27.8)	
Rare use	63 (24.5)	383 (38.3)	
Employment status, n (%)			<0.001 ^b
Employment (regular)/irregular	20 (7.8)	287 (28.7)	
Unemployed	237 (92.2)	712 (71.3)	
Social status, n (%)			<0.001 ^b
Homeless	26 (10.1)	36 (3.6)	
Not homeless	231 (89.9)	962 (96.4)	
Unknown	0	1	
TB contacts, n (%)			<0.001 ^b
Work/friends	5 (1.9)	52 (5.2)	
Unknown	246 (95.7)	864 (86.5)	
Family	6 (2.3)	83 (8.3)	
HIV, n (%)			<0.001 ^b
Unknown/negative	238 (92.6)	971 (97.5)	
Positive	19 (7.4)	28 (2.8)	
Substance use, n (%)			0.038 ^b
No/unknown	242 (94.2)	971 (97.2)	
Yes	15 (5.8)	28 (2.8)	
Place of residence, n (%)			0.837 ^b
Rural	114 (44.4)	436 (43.6)	
Urban	143 (55.6)	563 (56.4)	
Gender, n (%)			0.025 ^b
Female	50 (19.5)	262 (26.2)	
Male	207 (80.5)	737 (73.8)	
TB case category, n (%)			<0.001 ^b
New	146 (56.8)	723 (72.4)	
Relapse/return	111 (43.2)	276 (27.6)	
Tuberculosis resistance, n (%)			<0.001 ^b
Drug-resistance TB	75 (29.2)	449 (44.9)	
Multidrug-resistant TB	96 (37.4)	351 (35.1)	
Extensively drug-resistant TB	86 (33.5)	199 (19.9)	

^a, two sample *t*-test; ^b, Pearson's Chi-squared test. HIV, human immunodeficiency virus; N, negative; P, positive; SD, standard deviation; TB, tuberculosis.

Table S6 Demographic, clinical, and laboratory characteristics of the subsample study patients: univariate Firth's logistic regression

Risk factor	Patients (N=90)					
	Period I (N=30)		Period II (N=30)		Period III (N=30)	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Age (OR per 1-year increase)	1 (0.94–1.07)	0.972	1.07 (1.01–1.14)	0.018	0.97 (0.39–1.39)	0.401
Age (OR per 10-year increase) [†]	1.01 (0.53–1.89)	0.972	1.89 (1.11–3.59)	0.018	0.77 (0.39–1.39)	0.401
Aged 50 and above	0.79 (0.12–4.1)	0.79	18.82 (3.26–206.8)	<0.001	0.47 (0.09–2.07)	0.320
Low BMI (<18 kg/m ²)	14.49 (2.56–112.73)	0.002	3.1 (0.63–19.86)	0.169	7.86 (1.64–46.19)	0.009
Duration of hospitalization (OR per 30-day increase)	0.61 (0.37–0.94)	0.024	0.92 (0.76–1.09)	0.319	1.08 (0.98–1.21)	0.117
TB relapse	3.25 (0.68–17.68)	0.142	3.61 (0.87–16.74)	0.077	1.21 (0.28–5.35)	0.798
Male sex	1.97 (0.32–21.36)	0.484	2.23 (0.47–11.83)	0.312	0.8 (0.18–3.74)	0.774
Unsuccessful treatment, n (%)	8 (26.7)		16 (53.3)		10 (33.3)	

[†], the underlying variable is identical to that reported above; only the unit of increase (per 10 years) differs for interpretability of the odds ratio. OR, odds ratio; CI, confidence interval; BMI, body mass index.

Table S7 Demographic, clinical, and laboratory characteristics of the subsample study patients: multivariable Firth's logistic regression

Risk factor	Patients (N=90)					
	Period I (N=30)		Period II (N=30)		Period III (N=30)	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Age (OR per 1-year increase)	1.01 (0.92–1.11)	0.745	1.06 (0.99–1.14)	0.077	0.98 (0.91–1.05)	0.569
Age (OR per 10-year increase) [†]	1.16 (0.45–2.80)	0.745	1.73 (0.94–3.7)	0.077	0.82 (0.38–1.64)	0.569
Low BMI (<18)	7.8 (1.24–68.7)	0.028	1.87 (0.2–18.8)	0.564	5.62 (1.2–31.8)	0.029
Duration of hospitalization (OR per 30-day increase)	0.68 (0.37–1.13)	0.135	0.9 (0.7–1.09)	0.290	1.07 (0.95–1.24)	0.259
TB relapse	2.70 (0.41–21.8)	0.295	2.56 (0.56–13.01)	0.223	0.96 (0.14–6.29)	0.966
Male sex	0.76 (0.08–9.31)	0.809	1.25 (0.21–7.63)	0.801	0.53 (0.07–3.15)	0.487
Unsuccessful treatment, n (%)	8 (26.7)	–	16 (53.3)	–	10 (33.3)	–

[†], the underlying variable is identical to that reported above; only the unit of increase (per 10 years) differs for interpretability of the odds ratio. OR, odds ratio; CI, confidence interval; BMI, body mass index.